



TITLE:

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EFFECT OF ANTISERUM ON PERIPHERAL BLOOD LYMPHOCYTE

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Studies of ALS were started by Metchnicoff¹⁾ in 1899. Afterwards, Woodruff²⁾ and Anderson, Waksman, Arbouts, Jeejeebhoy²⁾ and Medawar³⁾ made remarkable progress in its studies. Starzl et al⁴⁾ used ALS clinically in the treatment of 11 renal recipients, and have advocated its effectiveness as one of the potent immunosuppressive agents. A case of renal allotransplantation was done in our clinic in February, 1969. The patient was a 28-year-old man with chronic nephritis and received an allograft from an unrelated living donor with idiopathic renal bleeding. Histocompatibility

tests performed on blood type, leucocyte type, MLC and NLT showed relatively good match. For immunosuppressive agents, azathioprine, predonine, ALS*, glycyrrhizin and local irradiation were employed. Dosages and ranges of the agents as well

* ALS used in our clinic was prepared by ammonium sulphate precipitation of the serum obtained from horses previously immunized against human spleen cells. The serum consists of r-globulin and T-equine globulin. Protein contents of serum is 4.90g/dl., and the leucoagglutinating titres against human white cells were 1:4,000 and the cytotoxicity titres were 2,000.

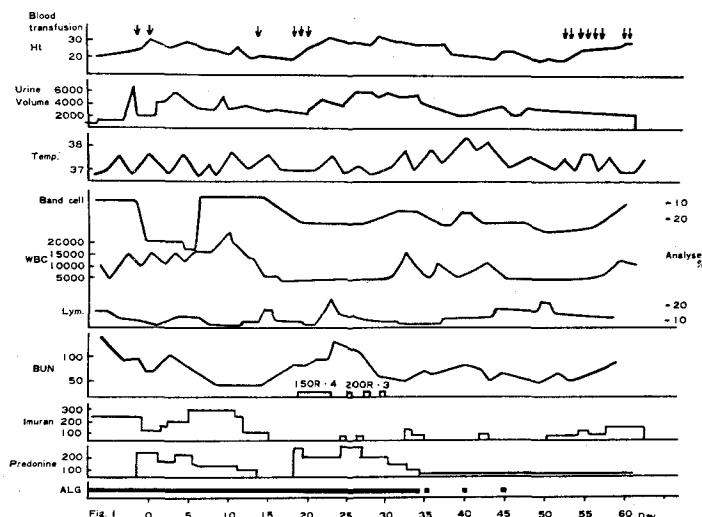


Fig. 1

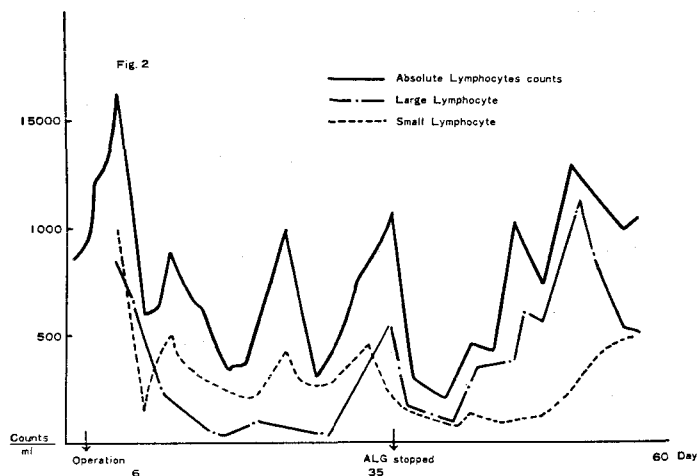


Fig. 2

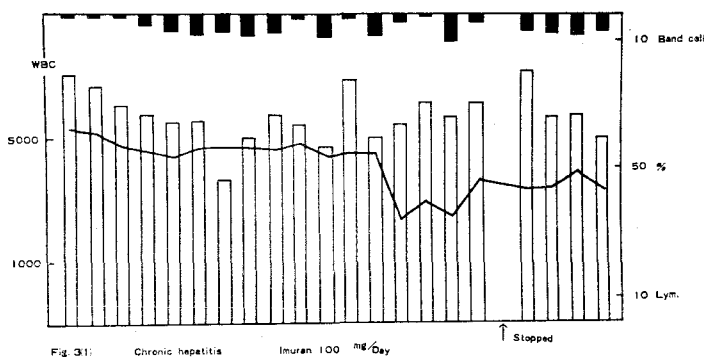


Fig. 3 (1)

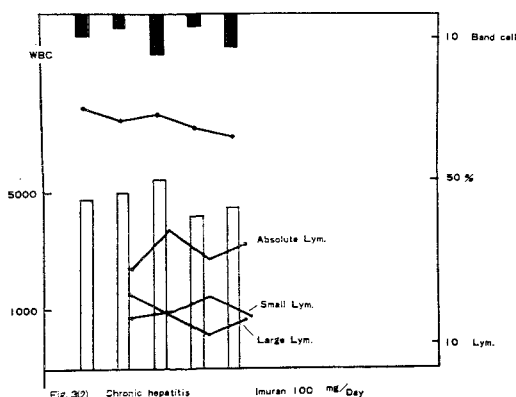


Fig. 3 (2)

as the clinical course are summarized in Fig. 1. Hemogram of the recipient was shown in the medium column of Fig. 1 and absolute lymphocyte count and their picture classified into large and small lymphocyte

were shown in Fig. 2.

Since it is generally thought that azathioprine depresses the granulocyte and that ALS depresses specifically the lymphocyte, control studies were done on three patients. Sole administration of azathioprine was done on two cases of chronic hepatitis and a case of nephrotic syndrome. Their hemograms were summarized in Fig. 3. It will be seen in the Fig. 1 and Fig. 3, by comparison, that azathioprine depletes the band cell neutrophils and the ALS mainly depletes the large lymphocytes. Here, a question has arisen whether depletion of large lymphocytes have an influence on the suppression of immunological reactions. As far as our case is concerned, no signs of

rejection were clinically apparent throughout the course. Possible mechanisms of action of ALS might be summarized as follows:

1. Lymphocyte depletion.
2. Interference with the immunologic process, e.g., by coating (blind folding) lymphocytic or their homograft targets.
3. Active interference in which ALS acts as a competitive antigens or by some form of sterile activation.
4. Other special mechanisms.

Immunologically competent cells are considered to be small lymphocytes. In our case, however, relations of small lymphocyte depletion to immunological reaction were again not apparent.

After ALS treatment was ceased, absolute lymphocyte counts increased, and you will see in the Fig. 2 that despite low small lymphocyte counts large lymphocyte counts

increased as absolute lymphocyte counts increase. Our ALS might be specifically sensitive to the large lymphocyte. However, the increase of large lymphocyte counts after cassation of ALS might be postulated as result of transformation of the small lymphocytes which were stimulated by the ALS and or immunological reactions in the host. Studies on the ALS specifically sensitive to small lymphocyte have been under way in our laboratory.

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末梢血中のリンパ球におよぼす ALS の影響

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移植時に用いられる免疫抑制剤にはプレドニン、イムラン、ALS、アスバラギナーゼなど種々あるが、そのどれをとっても適確な作用機序は残念ながら理解されていないのが現状である。一つにはまだ免疫反応の完全な解明がなされていないのがその原因である。

われわれは慢性腎不全患者に腎移植を施行し、免疫抑制剤にイムラン、プレドニン、ALS、局所レ線照射などを用いた。そのさい移植後

毎日常末梢血液像をみたが、ALSは大リンパ球に対して感受性があり、比較する意味で慢性肝炎の患者にイムランを使用し、これも毎日常末梢血液像をみたところイムランはリンパ球に対してほとんど感受性を持たず、多核白血球に感受性のあることがわかった。これらに対する免疫の意味づけは種々考えられるが、症例が少ないので、今後の症例および動物実験で解明する予定である。